

CLAIMS

1. A method of screening for and /or diagnosis of a cardiovascular disorder in a subject, comprising the steps of:
 - (a) detecting and /or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
 - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOs:1-2, 6-7, 11-12, 15-17, and 24-25;
 - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:1, 2, 11, 12, 15, 16, or 17;
 - iii) a variant, with at least 85% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:6, or 7;
 - iv) a variant, with at least 95% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:24, or 25; and
 - v) a fragment of a polypeptide as defined in i), ii), iii), or iv) above which is at least ten amino acids long; and
 - (b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control is indicative of a cardiovascular disorder.
2. A method of predicting a cardiovascular disorder in a subject, comprising the steps of:
 - (a) detecting and /or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
 - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOs:1-2, 6-7, 11-12, 15-17, and 24-25;
 - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:1, 2, 11, 12, 15, 16, or 17;
 - iii) a variant, with at least 85% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:6, or 7;
 - iv) a variant, with at least 95% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:24, or 25; and

- v) a fragment of a polypeptide as defined in i), ii), iii), or iv) above which is at least ten amino acids long; and
- (b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control indicates a risk of developing a cardiovascular disorder.

3. The method of claim 1 or 2, wherein the level of two or more of the polypeptides of claim 1 or 2 are detected and /or quantified in a biological sample from said subject.

4. The method of any one of claims 1 to 3, wherein said cardiovascular disorder is Coronary Artery Disease (CAD).

5. The method of any one of claims 1 to 4, wherein said biological sample is plasma.

6. The method of any one of claims 1 to 5, wherein said polypeptide is detected and /or quantified by mass spectrometry.

7. The method of any one of claims 1 to 5, wherein said polypeptide is detected and /or quantified by Enzyme-Linked Immuno Sorbent Assay.

8. An isolated polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOS:1-5, 6-10, 11-14, 15-23 and 24-28, wherein said polypeptide is fused to a heterologous polypeptide sequence.

9. An anti-Cardiovascular disorder Plasma Polypeptide (CPP) antibody that selectively binds to a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOS:1-5, 6-10, 11-14, 15-23 and 24-28.

10. A method of binding an antibody to a Cardiovascular disorder Plasma Polypeptide (CPP) comprising the steps of:

- i) contacting the antibody of claim 8 with a biological sample under conditions that permit antibody binding; and
- ii) removing contaminants.

11. The method of claim 10, wherein said antibody is attached to a label group.

12. The method of claim 10, wherein said sample is human plasma.

13. A method of identifying a Cardiovascular disorder Plasma Polypeptide (CPP) modulator comprising the steps of:

- i) contacting a test compound with a CPP comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOS:1-5, 6-10, 11-14, 15-23 and 24-28 under sample conditions permissive for at least one CPP biological activity;
- ii) determining the level of said at least one biological activity of the CPP;
- iii) comparing said level to that of a control sample lacking said test compound; and
- iv) selecting a test compound which causes said level to change for further testing as a CPP modulator for the prophylactic and/or therapeutic treatment of cardiovascular disorders.

14. A method of identifying a modulator of a cardiovascular disorder comprising the steps of:

- (a) administering a candidate agent to a non-human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder;
- (b) administering the candidate agent of (a) to a matched control non-human animal not predisposed to be affected or not being affected by the cardiovascular disorder;
- (c) detecting and /or quantifying the level of at least one polypeptide in a biological sample obtained from the non-human test of (a) or control animal of (b), wherein the at least one polypeptide is selected from:
 - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOS:1-2, 6-7, 11-12, 15-17, and 24-25;
 - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOS:1, 2, 11, 12, 15, 16, or 17;
 - iii) a variant, with at least 85% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOS:6, or 7;
 - iv) a variant, with at least 95% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOS:24, or 25; and
 - v) a fragment of a polypeptide as defined in i), ii), iii), or iv) above which is at least ten amino acids long; and
- (d) comparing the level of the at least one polypeptide of step (c); wherein an alteration in the level of the at least one polypeptide indicates that the candidate agent is a modulator of the cardiovascular disorder.

15. The method of claim 14, wherein the non-human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder comprises an increased plasma level of at least one of the polypeptides selected from:

- i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOs:1-2, 6-7, 11-12, 15-17, and 24-25;
- ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:1, 2, 11, 12, 15, 16, or 17;
- iii) a variant, with at least 85% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:6, or 7;
- iv) a variant, with at least 95% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:24, or 25; and
- v) a fragment of a polypeptide as defined in i), ii), iii), or iv) above which is at least ten amino acids long.

16. A method for monitoring the efficacy of a treatment of a subject having or at risk of developing a cardiovascular disorder with an agent, the method comprising:

- (a) obtaining a pre-administration biological sample from the subject prior to administration of the agent;
- (b) detecting and /or quantifying the level of at least one polypeptide in the biological sample from said subject, wherein the at least one polypeptide is selected from:
 - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOs:1-2, 6-7, 11-12, 15-17, and 24-25;
 - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:1, 2, 11, 12, 15, 16, or 17;
 - iii) a variant, with at least 85% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:6, or 7;
 - iv) a variant, with at least 95% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs:24, or 25; and
 - v) a fragment of a polypeptide as defined in i), ii), iii), or iv) above which is at least ten amino acids long; and
- (c) obtaining one or more post-administration biological samples from the subject;

- (d) detecting the level of the at least one polypeptide in the post-administration sample or samples;
- (e) comparing the level of the at least one polypeptide in the pre-administration sample with the level of the at least one polypeptide in the post- administration sample; and
- (f) adjusting the administration of the agent accordingly.